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Valve Thrombosis Following Transcatheter Aortic Valve Implantation: A Systematic Review

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ABSTRACT

Introduction and objectives: Despite the rapid global uptake of transcatheter aortic valve implantation, valve thrombosis has yet to be systematically evaluated in this field. The aim of this study was to determine the clinical characteristics, diagnostic criteria, and treatment outcomes of patients diagnosed with valve thrombosis following transcatheter aortic valve implantation through a systematic review of published data.

Methods: Literature published between 2002 and 2012 on valve thrombosis as a complication of transcatheter aortic valve implantation was identified through a systematic electronic search.

Results: A total of 11 publications were identified, describing 16 patients (mean age, 80 [5] years, 65% men). All but 1 patient (94%) received a balloon-expandable valve. All patients received dual antiplatelet therapy immediately following the procedure and continued to take either mono- or dual antiplatelet therapy at the time of valve thrombosis diagnosis. Valve thrombosis was diagnosed at a median of 6 months post-procedure, with progressive dyspnea being the most common symptom. A significant increase in transvalvular gradient (from 10 [4] to 40 [12] mmHg) was the most common echocardiographic feature, in addition to leaflet thickening. Thrombus was not directly visualized with echocardiography. Three patients underwent valve explantation, and the remaining received warfarin, which effectively restored the mean transvalvular gradient to baseline within 2 months. Systemic embolism was not a feature of valve thrombosis post-transcatheter aortic valve implantation.

Conclusions: Although a rare, yet likely under-reported complication of post-transcatheter aortic valve implantation, progressive dyspnea coupled with an increasing transvalvular gradient on echocardiography within the months following the intervention likely signifies valve thrombosis. While direct thrombus visualization appears difficult, prompt initiation of oral anticoagulation therapy effectively restores baseline valve function.

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Revisión sistemática de la trombosis protésica tras implante percutáneo de válvula aórtica

Resumen

Introducción y objetivos: A pesar de la rápida extensión del implante transcatheter de válvulas aórticas, la trombosis protésica tras la intervención es una complicación grave que no se ha evaluado sistemáticamente. El objetivo de este estudio es determinar las características clínicas, los criterios diagnósticos y el manejo de la trombosis protésica tras implante percutáneo de válvula aórtica mediante revisión sistemática de los datos publicados hasta la fecha.

Métodos: Se identificaron, mediante búsqueda electrónica sistemática, todos los artículos publicados en 2002-2012 relacionados con trombosis protésica como complicación tras implante percutáneo de válvula aórtica.

Resultados: Se identificaron 11 publicaciones que describían a un total de 16 pacientes (media de edad, 80 ± 5 años; el 65% varones) con trombosis protésica subaguda. En todos los casos excepto 1 (94%), se utilizaron prótesis de tipo balón expandible. Todos los pacientes recibieron doble antiagregación inmediatamente después del procedimiento y continuaban recibiendo al menos un antiagregante en el momento del diagnóstico, que se realizó una mediana de 6 meses tras el implante. La disnea progresiva fue el síntoma más común de presentación. El principal hallazgo ecocardiográfico fue un incremento en los gradientes transvalvulares (media de 10 ± 4 mmHg tras el implante a 40 ± 12 mmHg al diagnóstico), junto con el engrosamiento en las valvas. No se visualizaron directamente trombos mediante la ecocardiografía. En 3 casos la prótesis se sustituyó quirúrgicamente, mientras que el resto recibió warfarina, que consiguió un

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INTRODUCCIÓN

La trombosis peroperatoria (VT) tras intervención se asocia a la existencia de varios factores. En este estudio revisamos los datos publicados en los últimos 2 años sobreVT en el abordaje por medio del implante transcatéter de los prótesis de válvula aórtica.

RESULTADOS

Se revisaron 13 publicaciones relacionadas con los casos de VT, 3 de las cuales presentan datos de más de 100 pacientes. Los resultados se presentan en la tabla 1. Se destaca que el catéter se coloca distal al implante de la prótesis, lo que disminuiría el riesgo de VT en el primer año.

La comparación de resultados presentados en la tabla 1 con los de otros estudios permite establecer que se necesitan protocolos más estrictos para prevenir el desarrollo de VT.

CONCLUSIONES

La trombosis peroperatoria es un fenómeno frecuente que requiere un manejo adecuado para prevenirla. Se recomienda realizar un seguimiento cuidadoso de los pacientes para prevenir eventos tromboembólicos.

BIBLIOGRAFÍA


2. ASA: acetylsalicylic acid

3. OAC: oral anticoagulation

4. SAVR: surgical aortic valve replacement

5. TAVI: transcatheter aortic valve implantation

6. VT: valve thrombosis

7. INTRODUCTION

Valve thrombosis (VT) following surgical valve replacement is a life-threatening complication largely involving mechanical prostheses and is commonly associated with subtherapeutic oral anticoagulation (OAC) therapy.\(^1\) Bioprosthetic surgical aortic valves rarely thrombose, with an estimated incidence of 0.01% to 1.26%.\(^2\)\(^-\)\(^5\) Transcatheter aortic valve implantation (TAVI) is an established treatment for severe symptomatic aortic stenosis among patients whose surgical complication risk is deemed prohibitive or high.\(^6\) While thromboembolic complications of TAVI, particularly periprocedural cerebrovascular events, are well described,\(^7\)\(^-\)\(^9\) little is known of the occurrence of VT following TAVI. To date, an estimated 150 000 TAVI procedures or more have been performed worldwide. However, data on this critical complication is currently limited to isolated case reports or small case series, precluding a more formal evaluation of its chief clinical characteristics, management strategies, and outcomes.\(^10\)\(^-\)\(^22\) The objective of this systematic review is to provide further insight into the baseline characteristics, clinical presentation, management, and outcomes of patients diagnosed with VT following TAVI.

METHODS

A comprehensive and systematic search of all English-language articles in PubMed, Google Scholar, Cochrane Library, and BioMedCentral addressing thrombosis as a complication of TAVI was performed using the following keywords: “transcatheter aortic valve”, “transcatheter prostheses”, “TAVI”, “transcatheter aortic valve replacement”, “thrombosis”, “thrombus”, “dysfunction”, “obstruction”, “degeneration”, “stenosis”. A manual search was also performed of the major TAVI-related trials and registries. All publications were retrieved and evaluated independently by 2 investigators (J.G. Córdoba-Soriano and I. Amat-Santos). Articles reporting thrombosis of transcatheter valves in nonaortic positions were excluded. The data gathered included baseline demographics and clinical characteristics, diagnostic imaging, antithrombotic therapies post-TAVI, treatment of VT per se, and clinical outcomes. Echocardiographic data included left ventricular ejection fraction, valve area and gradients, and the presence of paravalvular leaks.

Statistical Analysis

Categorical variables are reported as No. (%) and continuous variables as mean (standard deviation) or median according to variable distribution. All analyses were performed with SAS version 9.2 (SAS Institute Inc.; Cary, North Carolina, United States).

RESULTADOS

Se buscaron 13 reportes describiendo 18 casos de trombosis como un complicación de TAVI que fueron identificados,\(^10\)\(^-\)\(^22\) incluyendo 2 individuos con tratamiento peroperatorio VT que se encuentran y descritos separadamente como “agudo” VT.\(^12\)\(^-\)\(^20\)

Tabla 1 describe las características basales y procedurales de los pacientes con VT post-TAVI. La edad media fue de 80 (5) años, con un menor antecedente. La fibrilación auricular no se reportó en ningún de los pacientes, y la fracción de eyecisión ventricular fue descripta en 5 pacientes. La coagulopatía fue diagnosticada en 10 pacientes (62%), uno de quienes presentó un 50% reducción en la proteína S actividad y un efecto positivo para la coagulación. Dos pacientes tenían una historia previa de stroke y 1 paciente se encontraba recogiendo OAC durante el procedimiento. La ausencia de enfermedad inflamatoria sistémica fue descrita en los pacientes previos y la relación con los componentes proasis se excluyó en 2 de ellos.

En todos los pacientes, TAVI se realizó a causa de severa estenosis valvular; este paciente se sometió al una trombosis-valvular procedimiento para el caso de un caso previo falta de implantación valvular progresivo. Se realizó en el paciente 1 (29%); 23 mm y 29 mm en 20% y 27% de los pacientes, respectivamente. Post-TAVI ecoangiografía demostró una media valvulográfica de 10 (4) mmHg y la presencia de una regurgitación residual fue reportada en 4 pacientes (29%). Todos los pacientes recibieron tratamiento antiplatélet en el post-TAVI, con dual antiplaquetaria (acetylsalicylic acid [ASA] + clopidogrel para 1–6 meses) siendo el más frecuente (86%) régimen. No paciente recibió OAC post-TAVI. La trombosis valvular fue eventualmente diagnosticado en un período de 6 (0,5–24) meses post-TAVI.

Tabla 2 describe la presentación clínica, los test diagnósticos, y los resultados de ecoangiografía en el momento de la presentación. La mayoría de los pacientes presentaron progresiva disnea, y 2 pacientes presentaron ataque isquémico cerebral. Los resultados de ecoangiografía fueron excluidos en todos los pacientes. Al momento de la presentación con VT, el 63% de los pacientes estaban siendo tratados con antitrombóticos: ASA monoterapia, 6 pacientes (38%); ASA + clopidogrel, 3 pacientes (19%); clopidogrel monoterapia, 1 paciente (6%). Dos pacientes (13%) no recibieron tratamiento antitrombótico en el momento de VT, y no datos de tratamiento antitrombótico se disponían en un total de 3 pacientes (19%). No paciente se encontraba recibiendo OAC al momento de VT.

Ecoangiografía reveló VT en la mayoría de los pacientes, caracterizado por un aumento en los gradientes transvalvulares (94% de pacientes), con un gradiente medio en el momento de VT diagnóstico de 43 (12) mmHg. Adicionalmente, aumentó el grosor valvular o restricción tabique subvalvular se describió en una muestra de pacientes, mientras que la ecoangiografía directa visualizó el trombo en el anillo.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>STS/EuroSCORE Risk factors</th>
<th>Valvulopathy Type of valve, size (mm)</th>
<th>Approach</th>
<th>Antithrombotic treatment</th>
<th>Time from implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>84</td>
<td>Female</td>
<td>1/22%</td>
<td>Severe AS</td>
<td>SAPIEN, 23 TA</td>
<td>ASA indefinitely, clopidogrel 6 months</td>
<td>No(^b) 6 months</td>
</tr>
<tr>
<td>2(^1)</td>
<td>78</td>
<td>Male</td>
<td>1/44%</td>
<td>Severe AS</td>
<td>SAPIEN, 26 TA</td>
<td>ASA indefinitely, clopidogrel 1 month</td>
<td>ASA 4 months</td>
</tr>
<tr>
<td>3</td>
<td>83</td>
<td>Male</td>
<td>5%/10% History of stroke</td>
<td>Severe AS</td>
<td>SAPIEN XT, 26 TF</td>
<td>ASA indefinitely, clopidogrel 6 months</td>
<td>ASA, clopidogrel 6 months</td>
</tr>
<tr>
<td>4(^1)</td>
<td>81</td>
<td>Male</td>
<td>3.9%/11%</td>
<td>Severe AS</td>
<td>SAPIEN XT, – TF</td>
<td>ASA, clopidogrel 3 months</td>
<td>ASA 15 months</td>
</tr>
<tr>
<td>5(^1)</td>
<td>83</td>
<td>Male</td>
<td>17%/20% History of stroke</td>
<td>Severe AS</td>
<td>SAPIEN XT, 26 TF</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6(^4)</td>
<td>80</td>
<td>Female</td>
<td>–/–</td>
<td>Severe AS</td>
<td>SAPIEN XT, 23 –</td>
<td>ASA, clopidogrel</td>
<td>ASA, clopidogrel 10 months</td>
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<tr>
<td>7(^4)</td>
<td>81</td>
<td>Male</td>
<td>–/–</td>
<td>Bioprosthetic dysfunction</td>
<td>SAPIEN XT, 23 –</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>8(^4)</td>
<td>74</td>
<td>Female</td>
<td>–/–</td>
<td>Severe AS</td>
<td>SAPIEN XT, 26 –</td>
<td>ASA, clopidogrel</td>
<td>–</td>
</tr>
<tr>
<td>9(^5)</td>
<td>74</td>
<td>Female</td>
<td>18.7%/–</td>
<td>Severe AS</td>
<td>SAPIEN, 23 TF(^c)</td>
<td>ASA &lt; 2 week</td>
<td>No</td>
</tr>
<tr>
<td>10(^6)</td>
<td>86</td>
<td>Male</td>
<td>–/7%</td>
<td>Severe AS</td>
<td>CoreValve(^a), 26 –</td>
<td>ASA indefinitely, clopidogrel 3 months</td>
<td>ASA 6 months</td>
</tr>
<tr>
<td>11(^7)</td>
<td>86</td>
<td>Male</td>
<td>–</td>
<td>Severe AS</td>
<td>SAPIEN XT, 29 –</td>
<td>ASA, clopidogrel</td>
<td>ASA, clopidogrel 1 week</td>
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<tr>
<td>12(^8)</td>
<td>81</td>
<td>Female</td>
<td>–/–</td>
<td>Severe AS</td>
<td>SAPIEN, 26 –</td>
<td>ASA</td>
<td>ASA 20 months</td>
</tr>
<tr>
<td>13(^9)</td>
<td>87</td>
<td>Male</td>
<td>15.6%/29%</td>
<td>Severe AS</td>
<td>SAPIEN XT, 29 TA</td>
<td>ASA indefinitely, clopidogrel 3 months</td>
<td>Clopidogrel(^d) 8 months</td>
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<tr>
<td>14(^11)</td>
<td>70</td>
<td>Male</td>
<td>–/–</td>
<td>Severe AS</td>
<td>SAPIEN XT, 26 TF</td>
<td>ASA indefinitely, clopidogrel 1 month</td>
<td>ASA 6 months</td>
</tr>
<tr>
<td>15(^2)</td>
<td>–</td>
<td>–</td>
<td>–/–</td>
<td>Severe AS</td>
<td>SAPIEN XT, 29 TA</td>
<td>UFH 5 days, ASA indefinitely, clopidogrel 12 months</td>
<td>ASA 3 months</td>
</tr>
<tr>
<td>16(^2)</td>
<td>–</td>
<td>–</td>
<td>–/–</td>
<td>Severe AS</td>
<td>SAPIEN XT, 29 TA</td>
<td>UFH 5 days, ASA indefinitely, clopidogrel 12 months</td>
<td>ASA 4 months</td>
</tr>
</tbody>
</table>

**Acute thrombosis cases**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>STS/EuroSCORE Risk factors</th>
<th>Valvulopathy Type of valve, size (mm)</th>
<th>Approach</th>
<th>Antithrombotic treatment</th>
<th>Time from implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>17(^12)</td>
<td>66</td>
<td>Male</td>
<td>–/–</td>
<td>Severe AS</td>
<td>SAPIEN, 23 TF</td>
<td>UFH, ASA, clopidogrel</td>
<td>Acute</td>
</tr>
<tr>
<td>18(^20)</td>
<td>90</td>
<td>Male</td>
<td>17%/–</td>
<td>Severe AS</td>
<td>SAPIEN, 26 TF</td>
<td>UFH, ASA, clopidogrel</td>
<td>Acute(^e)</td>
</tr>
</tbody>
</table>

AS, aortic stenosis; ASA, acetylsalicylic acid; PAF, paroxysmal atrial fibrillation; PE, pulmonary embolism; STS, Society of Thoracic Surgeons; TA, transapical; TF, transfemoral; UFH, unfractionated heparin.

\(^a\) Mild reduction of protein S activity (30%) and positive cold agglutinins were detected.
\(^b\) The patient discontinued the treatment.
\(^c\) Performed across an iliac conduit.
\(^d\) Patient discontinued acetylsalicylic acid due to recurrent epistaxis.
\(^e\) Hydrophilic polymer embolism-induced acute thrombosis. Cardiac arrest 18 h following the procedure.
patients appeared elusive. Computed tomography was performed in 5 patients, however, and revealed hypodense structures compatible with thrombus.

Table 3 describes the clinical management of VT. No patient underwent thrombolysis, and most patients (78%) received OAC therapy, with 3 patients undergoing surgical replacement. Concomitant antiplatelet therapy was reported in 4 patient. Mean transvalvar gradients were successfully reduced by OAC at a median time of 2 (1-10) months. A definitive diagnosis of VT was made in 5 patients following direct visualization at surgery or

ASA, acetylsalicylic acid; LMWH, low molecular weight heparin; UFH, unfractionated heparin; VKA, vitamin K antagonist.
during post-mortem examination, whereas the remaining cases were considered VT following significant reductions in transvalvular gradients during OAC therapy.

**Acute Valve Thrombosis Post-transcatheter Aortic Valve Implantation**

Two cases of VT occurred acutely following transfemoral TAVI with a first-generation Edwards SAPIEN valve. Both patients had received preprocedural dual antiplatelet therapy in addition to periprocedural unfractionated heparin. One case involved preprocedural discontinuation of OAC, initially prescribed for low left ventricular ejection fraction pre-TAVI. Following valve implantation, echocardiography revealed thrombus adhering to the stent frame in each patient. In both patients, unfractionated heparin was continued and in 1 particular patient, attempts at manual thrombus aspiration proved unsuccessful.

**DISCUSSION**

Bioprosthetic valves are generally considered less thrombogenic than their mechanical counterparts, in many instances obviating the need for long-term OAC. Nevertheless, the risk of thromboembolic events is not insignificant, particularly within the first 3 months following surgical aortic valve replacement (SAVR).23,24 The incidence of VT following SAVR is estimated to range from 0.03 events per 100 patient-years,25 with reports of a 15-year incidence of 0.37% to 26%.26 Since the inception of TAVI in 2002,27 and despite an estimated 150,000 procedures or more having now been performed worldwide, large-scale clinical trials and registries have formally reported a single VT case.28–38 Moreover, a number of isolated clinical descriptions of VT post-TAVI coupled with largely empiric peri- and post-procedural antithrombotic regimens following TAVI underscores the importance of a timely systematic review of this poorly described phenomenon.

Several pertinent findings have emerged from this systematic review:

- Most VT cases occurred within 1 year after TAVI, with a median time of onset of 6 months.
- Almost all patients described gradual onset of increasing dyspnea, with the absence of clinical embolism. Although direct thrombus visualization was not described with echocardiography, suggestive echocardiographic morphological features included reduced leaflet mobility, increased leaflet thickening, and progressively increasing transvalvular gradients.
- A preponderance of VT cases post-TAVI occurred following balloon-expandable valve implantation.
- Valve thrombus post-TAVI was successfully treated following prompt OAC therapy, effectively restoring transcatherer valve function and hemodynamic performance.

**Clinical Presentation and Diagnostic Tools**

Following the initial symptom relief after TAVI for severe aortic stenosis, increasing dyspnea coupled with a progressively rising transvalvular gradient was a near universal finding among patients with VT post-TAVI. These findings appear analogous to the nature and timing of VT post-SAVR utilizing bioprostheses.2–5 The median time following TAVI for the diagnosis of VT was 6 months, with most cases being diagnosed within 1-year post-TAVI. This compares with a peak incidence for surgically-implanted aortic bioprostheses occurring at 13 months to 24 months reported by Pislaru et al4 and a median time of 12 months post-SAVR reported by both Brown et al39 and Jander et al.40 The immediate implications of the present findings relate to promoting a heightened clinical awareness for the possibility of VT post-TAVI, particularly among patients with worsening dyspnea following TAVI. An important observation was that direct visualization of a valve-related thrombus seems not to be a requirement for diagnosis and management. Rather, in patients with an elevated (or rising) echocardiographic transvalvular gradient, the diagnosis of VT should be strongly suspected, rather than simply valve degeneration. Whilst computed tomography imaging may provide supportive visual evidence of thrombus, this should not preclude the initiation of OAC (at the expense of antiplatelet therapy) as an effective means of eradicating TAVI-related VT. Interestingly, transesophageal echocardiography seemed unable to clinch the diagnosis of VT in many of the reported cases.

Currently, no formal clinical criteria exist for diagnosing VT post-TAVI. Pislaru et al4 proposed, from their series of surgically implanted aortic bioprostheses, that an increase in transvalvular gradient of > 50% from baseline within 5 years following SAVR (in the absence of increased flow), coupled with the presence of thickened/immobile cusps (or the presence of an overt mobile mass) should signify the likely presence of VT.41 However, direct exclusion of these criteria from TAVI population without formal, prospective evaluation may be somewhat premature. Importantly, these criteria should not currently serve as a barrier for implementing OAC therapy in patients strongly suspected of having VT following TAVI.

**Prevention and Management of Valve Thrombosis Post-transcatheter Aortic Valve Implantation**

Following SAVR with a bioprosthetic valve, various treatment guidelines are concordant in recommending ASA or OAC therapy during the initial 3 months after surgery, followed by long-term ASA monotherapy.40,41 However clinical practice remains heterogeneous.42–46 probably because such guidelines are essentially based on observational, retrospective data.23,24,47–48 Following TAVI, dual antiplatelet therapy (ASA + clopidogrel) is currently recommended and used in most centers, but the duration of clopidogrel varies widely among studies (ranging from 1 month to 6 months).49 This lack of consensus is reflected by the significant heterogeneity of post-TAVI antithrombotic management described among VT cases in the present review, whereby 57% of patients were receiving ASA monotherapy and 21% were receiving dual antiplatelet therapy at the time of VT diagnosis. Merie et al50 noted a reduced risk of thromboembolic events and cardiovascular death with OAC therapy in the immediate 6-month period following SAVR with bioprosthetic valves. Clinical guidelines stipulate that thromboembolic risk factors such as atrial fibrillation, left ventricular systolic dysfunction, prior thromboembolism, and a known hypercoagulable state are important reasons for considering OAC following surgical aortic bioprosthetic valve deployment.50,51 Six (38%) patients in the present VT post-TAVI cohort had risk factors for thrombosis. This highlights the importance of an individualized approach for post-TAVI thromboembolic prophylaxis. Future studies, such as the ongoing ARTE (Aspirin versus Aspirin Clopidogrel Following Transcatheter Aortic Valve Implantation) pilot trial (NCT01559298) should provide key data informing future large-scale, clinical trials.

While traditional definitive management strategies of VT following SAVR encompassed either repeat surgery or thrombolysis, these treatment options involve considerable risk.39,50,51 Most patients with TAVI-related VT were successfully managed with
OAC therapy, and these patients experienced significant clinical and hemodynamic improvement, with normalization of transvalvular gradients after 2 months of OAC therapy. These findings appear analogous to the successful use of OAC therapy for treating VT in the bioprosthesis SAVR or mitral valve population.3,19,51 Collectively, these findings support the rationale for commencing OAC therapy in post-TAVI patients suspected to harbor VT, including those with progressive dyspnea, valve leaflet thickening, restricted leaflet mobility, and a progressively rising echocardiographic transaortic gradient. The duration of OAC, however, remains unclear and should be determined on an individual basis. In the event of OAC cessation, we recommend institution of dual antiplatelet therapy and frequent echocardiographic surveillance.

**Differing Thrombosis Rates Across Balloon vs Self Expanding Transcatheter Aortic Valves**

Most VT cases were reported following balloon-expandable valve implantation. Although it is difficult to determine the precise mechanisms underscoring these observations, it is likely that VT post-TAVI relates to the complex interplay of a number of patient-, procedural-, and valve-related phenomena. Both the Edwards SAPIEN and CoreValve® are stented pericardial valves incorporating bovine and porcine tissue, respectively.6,52 However, the stented-frame design and composition of each valve differs substantially; the CoreValve® is longer and nitinol-based compared with the shorter and stainless steel or cobalt-chromium-based Edwards SAPIEN valve. It is plausible that the metallic frame could serve as a nidus for thrombus, particularly until complete endothelialization occurs, which could take up to 12 months or more.6,53,54 Additionally, the Edwards SAPIEN valve contains a polyethylene terephthalate skirt, designed to minimize paravalvular regurgitation, not present on the CoreValve®. Nevertheless, Ducci et al55 observed in vitro that both transcatheter aortic valve designs result in reduced sinus of Valsalva flow, contributing to relative blood stasis on the aortic side of the valve. Compounding these valve-related hemodynamic factors is the likely occurrence of native valve leaflet fissuring, perforation, and endothelial denudation following balloon dilatation prior to balloon-expandable TAVI, providing additional stimuli for a localized prothrombotic milieu.

**Limitations**

Several limitations of the current review warrant consideration. The present analysis is likely to be affected by reporting/publication bias, thus limiting an accurate estimation of the true incidence of VT after TAVI and its clinical characteristics. This furthermore precludes any meaningful conclusions of the differing rates of VT across balloon expandable vs self-expanding valve designs. An added degree of reporting bias is likely to be present in the large number of patients who died at varying time intervals following TAVI and who did not undergo formal diagnostic evaluation or post-mortem examination either prior to or following death. Additionally, other clinical associations (ie, atrial fibrillation, thrombophilia, etc) may not have been systematically reported or assessed. Despite this, the present systematic review serves as an original collective summary of an important, preventable, and treatable complication following TAVI.

**CONCLUSIONS**

As the global uptake of TAVI for treating severe aortic stenosis remains exponential, rare complications of this evolving treatment paradigm will continue to be encountered more frequently. Given the present uncertainty of the optimal peri- and post-procedural antithrombotic regimen during TAVI, clinicians should have a heightened awareness of VT following TAVI. The direct visualization of thrombus is not necessary for a diagnosis of VT following TAVI. Rather, in patients with progressive dyspnea and a rising echocardiographic transaortic gradient, OAC therapy may be an effective means of restoring normal valve function.

**CONFLICTS OF INTEREST**

J. Rodés-Cabau and E. Dumont are consultants for Edwards Lifesciences. J.G. Córdoba-Soriano received support from Abbott Vascular and Fundación Biotyc, Albacete, Spain.

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